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Attached hereto is a marked-up version of the changes made to the Specification by the current Amendment. The attached pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Specification:**

Paragraph beginning at line 14 of page 21 has been amended as follows:

PDZ domains of proteins are named after three prototypical proteins: PSD95, Drosophila large disc protein and Zonula Occludin 1 protein (Gomperts et al., 1996, *Cell* 84:659-662). PDZ domain-containing proteins are involved in synapse formation by organizing transmembrane neurotransmitter receptors through intracellular interactions. PDZ domains contain the signature sequence GLGF (SEQ ID NO:29). In the nervous system, typical PDZ domain-containing proteins contain three PDZ domains, one SH3 domain and one guanylate kinase domain. Examples of intracellular PDZ domain-containing proteins include LIN-2, LIN-7 and LIN-10 at the pre-synapse, and PSD95 at the post-synapse.

Paragraph (TABLE 2) beginning at line 1 of page 26 has been amended as follows (see attached sheets).

Paragraph (TABLE 3) beginning at line 1 of page 33 has been amended as follows (see attached sheets).

Paragraph beginning at line 25 of page 50 has been amended as follows:

As noted *supra*, PCR primers were designed to include endonuclease restriction sites to facilitate ligation of PCR fragments into a GST gene fusion vector (pGEX-3X; Pharmacia, GenBank accession no. XXU13852) in-frame with the glutathione-S transferase coding sequence. This vector contains a IPTG inducible lacZ promoter. The pGEX-3X vector was linearized using *Bam* HI and *Eco* RI or, in some cases, *Eco* RI or *Sma* I, as shown in TABLE 3, and dephosphorylated. For most cloning approaches, double digest with *Bam* HI and *Eco* RI was performed, so that the ends of the PCR fragments to clone were *Bam* HI and *Eco* RI. In some cases, restriction endonuclease combinations used were *Bgl* II

## PDZ-LIGAND/PDZ INTERACTION SUMMARY

TABLE 2

PDZ LIGAND	CODE	SEQ	SEQ ID NO.	CASK	MPP1	DLG1	PSD95	NeDLG	TAX33	SYN1a	TAX 43	LDP	LIM	LIMK1	LIMK2	MPP2
CD6	AA6L	ISAA	14													
CD49E (alpha-4)	AA11L	TSDA	24													
CD49F (Alpha, alpha6)	AA12L	TSDA	24													
CD166 (CD6L)	AA20L	KTEA	64													
CD148	AA55L	KTIA	278													
CC CKR-2	AA42L	KEGA	283													
CD138 (syndecan)	AA18L	EFYA	89	*												
CD148 (DEP-1)	AA19L	GYIA	119													
CD98 (2F4)	AA15L	PYAA	54													G
CLASP-1	AA1L	SAEV	284			G	A	G								
CLASP-4	AA3L-V	YAEV	228			A	A	A				A				
NMDA	AA34.2L	ESDV	263		A	A/G	A/G	A/G		G	A		A			G
VCAM1	AA17L	KSKV	163		A	A		A				A				
CLASP-2	AA2L	SSVV	223			A/G	A/G	A/G								
CD95 (Apo-1/Fas)	AA13L	QSLV	44			A/G	A/G	A/G								
KV1.3	AA33L	FTDV	238			A/G*	A/G*	A/G					A			
DNAM-1	AA22L	KTRV	74		A	A	A/G	A				A				G
CD63	AA47L	TELV	248			A	A	A								
CD44 (long form)	AA9L	KIGV	104		G											
Neurexin	AA38L	EYVV	268	G*	A*	A/G	A/G	G		A	A		A			
CD97 (CD55L)	AA14L	ESGI	49			A										
Glycophorin C	AA37L	EYFI	273	*	G	G	G									A
CDW128A (IL8RA)	AA29.1L	SSNL	69			A		A								
CD3n	AA4L	SSQL	4			A	A									
LPAP	AA30L	VTAL	84			A										
CD46 (form 1)	AA10L	FTSL	109			A/G	A/G	G								
CDW128B (IL8RB)	AA29.2L	STTL	233			A/G	A	A/G								
DOCK2	AA40L	STDL	243			A	A/G	G		G						
CD34	AA7L	DTEL	149			A	A	G								
CD5	AA49L	AQRL	285													
CC CKR-4	AA44L	HDAL	286													
FceRIB	AA25L	PIDL	129													
FasLigand	AA23L-M	LYKL	79													
CD62E	AA48L	SYIL	168													
CC CKR-1R	AA41L	SAGF	287													
CDW125 (IL5R)	AA28L	DSVF	94													
BLR-1	AA45L	LTTF	253													
CC CKR-3	AA43L	SIVF	288													
				CASK	MPP1	DLG1	PSD95	NeDLG	TAX33	SYN1a	TX 43	LDP	LIM	LIMK1	LIMK2	MPP2

\* Interactions described in the scientific literature

**PDZ-LIGAND/PDZ INTERACTION  
SUMMARY**

**TABLE 2  
CONTINUED**

NOS1	AF6	PTN-4	prIL16	41.8	K559	RGS12	K316	DVL1	TAX 40	TIAM1	MINT1	K303	CBP	MINT3	TAX 2	K561	PDZ LIGAND
				A													CD6
				A/G													CD49E (alpha-4)
				A/G													CD49F (Aform, alpha6)
																	CD166 (CD6L)
																	CD148
																	CC CKR-2
				A/G						A							CD138 (syndecan)
																	CD148 (DEP-1)
																	CD98 (2F4)
																	CLASP-1
				A							A						CLASP-4
				A/G							A/G				A	G	NMDA
					A/G					A							VCAM1
					A						A						CLASP-2
					A												CD95 (Apo-1/Fas)
					A/G												KV1.3
					A												DNAM-1
					A												CD83
					A												CD44 (long form)
					A												Neurexin
					A												CD97 (CD55L)
					A												Glycophorin C
					A												CDW128A (IL8RA)
					A/G												CD3n
																	LPAP
																	CD46 (form 1)
																	CDW128B (IL8RB)
																G	DOCK2
																	CD34
																	CD5
																	CC CKR-4
																	FcεRb
																G	FasLigand
																	CD62E
																	CC CKR-1R
																	CDW125 (IL5R)
																	BLR-1
																	CC CKR-3
NOS1	AF6	PTN-4	prIL16	41.8	K559	RSG12	K316	DVL1	TX 40	TIAM1	MINT1	K303	CBP	MINT3	TX 2	K561	

\* Interactions described in the scientific literature

TABLE 3  
PDZ DOMAINs

Key:

Gene names and corresponding gene products are provided. In some cases, cDNA sequences representing the same gene have several database entries under different accession numbers and names. Accession numbers shown correspond to the gene name used in this description, and numbering of nucleotides and amino acids correlates to those Genbank entries. Amino acid sequences shown correspond to the cloned DNA portions of PDZ domain containing genes. Linker amino acid sequences (e.g., amino acids encoded by DNA flanking the cloning site of the pGEX-3X cloning vector) are in italics

GENE SYMBOL	PROTEIN	ACC.#	AMINO ACID SEQUENCE*	CLON. SITES	FORWARD PRIMER	REVERSE PRIMER
CASK	CASK	Y17138	AA495-584; PDZ domain 1 (of 1)	Bam HI / Eco RI	6CAF 5' - TCGGATCCAT GTGACCAAG TTCGG-3' <u>(SEQ ID NO:322)</u>	7CAR 5' - TCGGAATTCA ACTGAGTGC GA TA-3' <u>(SEQ ID NO:323)</u>

MPP1	55 Kd erythrocyte membrane protein	M64925	AA101-186; PDZ domain 1 (of 1)  RKVRLIQFEKVKTEEPMGITLKLH EKQSCVTAVRILHGGMIHRQGSLH VGDEILEINGTNVTNHSVDQLQK AMKETKGMSLKVIPNQREFIVT D (SEQ ID NO:293)	Bam HI / Bam HI 5' - GGGATCCGGA AAGTGCAC CATAC-3' (SEQ ID NO:324)	62MPF 63MPR 5' - ACGGATCCGCT GGTTGGGAATT ACTT-3' (SEQ ID NO:325)
DLG1	human homolog of Drosophila discs large protein	U13897	AA275-477; PDZ domains 1-2 (of 3)  QVNGETADYEEITLERGNGL GFSIAGGTDDNPHIGDDSSIFITK IITGGAAAQDGRLRVNDCILQVN EVDVDVTHSKAVEALKEAGSIV RLYYVKKRRKPVSEKIMEIKLIKGP KGLGFSIAGGVGNQHI PGDNSTY VTKIIEGGAAHKDGLQIGDKLL AVNNVCLLEEVTHEEAVTALKNTS DFVYLKVAKPTSMYMMNDGYAPNS S (SEQ ID NO:294)	Bam HI / Eco RI 5' - TCGGATCCAG GTTAATGGCT CAGATG-3' (SEQ ID NO:326)	2DR 5' - CGGAATTCCGGT GCATAGCCATC -3' (SEQ ID NO:327)

PSD95	human post-synaptic density protein 95	U83192	AA387-724 ; PDZ domains 1-3 (of 3)	Bam HI / Eco RI	8 PSF 5' - TCGGATCC TT GAGGGGAGA TCGGAATT CGC TATACTCT CT GG - 3' <u>(SEQ_ID NO:328)</u>	11 PSR 5' - TCGGATCC TT GAGGGGAGA TCGGAATT CGC TATACTCT CT GG - 3' <u>(SEQ_ID NO:329)</u>
			<p>LEGEGERMEYEETLERGNGLGF SIAGGGTDNPHEGDDPSIFITKII PGGAAQAQDGRLLRVNDSIILFVNNEV DVREVTTHSAAVEALKEAGSIVRL YVMRRKPPAEKVMEIKLIKGPKG LGFSIAGGGVGNQHIPGDNSIYVT KLIEGGAAHKDGRILQIGDKILAV NSVGLEDMHEDAVAALKNTYDV VYLKVAKPSNAYLSDSYAPPDIT TSYSQHLDNEISHSSYSLGTDYPT AMTPTSPRRYSPVAKDLLGEEDI PREPRRIVIHRGSTGLGFNIYGG EDGEGLFISFILAGGPADLSGEL RKGDQILSVNGVDLNRNASHEQAA IALKNAGQTVTIIAQYKPEFIV <u>(SEQ_ID NO:295)</u></p>	N1150-1173	N2191-2168	

NedLG	presynaptic protein sao102 (neuroendo-crine-dlg)	U49089	AA205-1171; PDZ domains 1-2 (of 3)	Bam HI / Eco RI	71NEDF	72NEDR
			QYEEIVLERGNNSGLGFSIAGGID NPHVPPDDPGIFITKTIPIGGAAAM DGRLLGVNDCVLRVNNEVESEVVH SRAVEALKEAGPVVRLVVRRRQP PPETIMEVNLLKGPKGJGFESIAG GIGNQHIPGDNSIYITKIIEGGA AQKDGRLLQIGDRLLAVNNTNLQD VRHEEAVASLKLNTSDMVYLKVAK PGSPR <u>(SEQ ID NO:296)</u>	5' - CAGGATCCA TATGAGGAA TCGTACTTG- 3' <u>(SEQ ID</u> <u>NO:331)</u>	5' - TTGAATTGAG GCTGCCTGGCT TGGC-3' <u>(SEQ ID</u> <u>NO:331)</u>	
TAX33	tax interaction protein 33	AF028826	AA73-162; PDZ domain 1 (of 1)	Bam HI / Eco RI	92TAF	93TAR
			HSHPRVVELPKTDEGLGFNVMGG KEQNSPIYISRIIPGGVAERHGG LKRGDQLLSVNGVSVEGEHHHEKA VELLKAAKDSVKLVVRYTPKVLE FIVTN <u>(SEQ ID NO:297)</u>	5' - GTGGGATCCA CTCCCACCC CGAGTAG-3' <u>(SEQ ID</u> <u>NO:332)</u>	5' - CATGAATTCCA GAACCTTTGGG TGTATCGC-3' <u>(SEQ ID</u> <u>NO:333)</u>	
					N208-234	N497-468

SYN 1 α	alpha1-syntrophin	U40571	AA96-189 PDZ domain 1 (of 1)	Bam HI / Eco RI	124SYF	125SYR
			QRRRVTVRKADAGGLGISIKGGR ENKMPILISKIFKGLAADQTEAL FVGDAILSVNGEDLSSATHDEAV QVLKKTGKEVVLEVVKYMDVSPY FKNSSS <u>(SEQ ID NO:298)</u>	5' - TACGGATCCA GCCGCCGCC CGTGAC-3' <u>SEQ ID</u> <u>NO:334)</u>	5' - GTAGAATTCTT GAATAACGGTG AGAC-3' <u>SEQ ID</u> <u>NO:335)</u>	

TAX43	human tax interaction protein 43	AF028828	AA15-85 PDZ domain 1 (of 1)	Bam HI / Eco RI	97TAF	98TAR
			QKRGVVKVLKQELIGGLGISIKGKG ENKMPILISKIFKGLAADQTOAL YVGDAILSVNGADLIRDATHDEAV QALQFIVTN <u>(SEQ ID</u> <u>NO:299)</u>	5' - TCTGGATCCA GAAGCGTGGC GTGAAGG-3' <u>SEQ ID</u> <u>NO:336)</u>	5' - CGGAATTCAAC GCCTGCACCGC CTC-3' <u>SEQ ID</u> <u>NO:337)</u>	N267-231

LDP	Lim domain protein clp-36	U90878	AA46-88 PDZ domain 1 (of 1)	Bam HI / Eco RI	146LIF	147LIR
			RGMTTQQIDLQGPWPWGFRLVGR KDFEQPLAISRVTPGSKAALASS <u>(SEQ ID NO:300)</u>		5' - CAGGATCCG CGGAATGACC ACCCAGC-3' <u>(SEQ ID NO:338)</u>	5' - CATGAATTTCGC TAGAGCCGCC TGCTT-3' <u>(SEQ ID NO:339)</u>
					N129-155	N276-239
LIM	Human LIM protein	AF061258	AA29-112; PDZ domain 1 (of 1)	Bam HI / Eco RI	182LIF	183LIR
			LSNYSVSLVGPAPWGFRLQGGKD FNMPLTSSLKDGKAAQANVRI GDVVLSIDGINAQGMTHLEAQNK IKGCTGSLLNMTLQRASC <u>(SEQ ID NO:301)</u>		5' - TTAGGATCCT GAGCAAGTAC AGTGTGTAC -3' <u>(SEQ ID NO:340)</u>	5' - CTTGAATTTCAG CAGATGCTCT TGCAGAGTC- 3' <u>(SEQ ID NO:341)</u>
LIMK1	human LIM domain kinase 1	NM_002314	AA1194-291; PDZ domain 1 (of 1)	SMA I	52LIFF	53LIIP
			TVTLVSIPASSHGKRGILSVS1DP PHGPPGCCTEHSHTVRQGVDPG CMSPDVKNSSIHVGDRILEINGTP IRNVFLDEIDLIIQETSRLLQLT LEHDPGIHRD <u>(SEQ ID NO:302)</u>		5' - CTGCCCCGGGA CCGTACCCCT GGTGTCC-3' <u>(SEQ ID NO:342)</u>	5' - TCGCCCCGGTC ATGCTCGAGGG TC-3' <u>(SEQ ID NO:343)</u>
					N570-597	N874-851

LIMK2	human LIM domain kinase 2	D45906	AA185-275; PDZ domain 1 (of 1)	Bam HI / Eco RI	185LF	186LR
			PYSVTLISMPATTEGRRGFSVSV ESACSNYATTQVKEVNRMHISP NNRNAIHPGDRILEINGTPVRTL RVEEEVEDAISQTSQLLIEHE FIVTN <u>(SEQ ID NO:303)</u>	5' - AGCGGATCCC CTACTCTGTC ACGCTCATC- 3', <u>(SEQ ID NO:344)</u>	GACGAATTCACT GTTCAATCAAC AGCTGAAG-3', <u>(SEQ ID NO:345)</u>	5' -
MPP2	maguk p55 subfamily member 2 (DLG2)	X82895	AA185-273; PDZ domain 1 (of 1)	Bam HI / Eco RI	142MF	143MR
			QPVPPDAVRMVGIRKTAGEHLGV TFRVERGGELVIARIILHGMVAQQ GLLHVGDIIKEVNGQPVGSDPRA LQELLRNASGSVILKILPNYQVF IVTD <u>(SEQ ID NO:304)</u>	5' - TCAGGATCCA GCCGTGTACCT CCGATGC- 3', <u>(SEQ ID NO:346)</u>	ATGGAATTCC GGTAGTTGGGC AGGATC-3', <u>(SEQ ID NO:347)</u>	5' -

NOS1	human neuronal nitric oxide synthase	U17327	AA239-988; PDZ domain 1 (of 1)	Bam HI / Eco RI	155NOF	156NOR
			IOPNVISVRLFKRKVGGGLGFLVK ERVSKPPVIIISDLIRGGAAEQSG LIQAGDIIILAVNGRPLVDLSDS ALEVLRGIASETHVVLLLRGPEF IVTD <u>(SEQ_ID NO:305)</u>	5' - AGCGGATCCA GCCCAATGTC ATTTC- 3' <u>(SEQ_ID</u> <u>NO:349)</u>	5' - GAAGAATTTCAG GGCCCTTACAGA ATG- 3' <u>(SEQ_ID</u> <u>NO:349)</u>	
AF6	af-6 protein	U02478	AA985-1077; PDZ domain 1 (of 1)	Bam HI / Eco RI	66AFF	67AFR
			LRKEPEIITVTLLKKQNGMGLSIV AAKGAGQDKLIGIYVKSVVKGAA DVDGRLAAGDQLLSVDGRSLVGL SQERAELMTRSSVVTLEVAKQ GEFIVTD <u>(SEQ_ID NO:306)</u>	5' - TCGGATCCTG AGAAAAAGAAC CTGAA- 3' <u>(SEQ_ID</u> <u>NO:350)</u>	5' - TAGAATTCAACC CTGCTTTGCTA CTTC- 3' <u>(SEQ_ID</u> <u>NO:351)</u>	
					N2946-2970	N3239-3214

PTN-4	protein-tyrosine phosphatase meg1	M68941	AA774-862; PDZ domain 1 (of 1)	Bam HI / Eco RI 5' -	247PTF ATCGAATTTCAG CATTAGGTGCA ACTAG - 3' <u>(SEQ ID NO: 353)</u>	248PTR 5' -
prIL16	putative interleukin 16 precursor	S81601	AA1170-383; PDZ domain 1-2 (of 2)	Bam HI / Eco RI 5' -	75PRF ACGGGATCCA TGTCAACCAC TTACAC - 3' <u>(SEQ ID NO: 354)</u>	76PRR 5' -

41.8 kD	hypotheti- cal 41.8 kD protein	AF007156	AA4-85; PDZ domain 1 (of 1)	Bam HI / Eco RI	145HF	146HR
	RDSGAMLGLKVGGKMTESGRLLC AFITKVKKGSILADTVGHLRPGDE VLEWNGRLLQQGATFEEVYNILLE SKPEPQVELVVSRA NSS <u>(SEQ ID NO:309)</u>			5' - GTGGGATCCG AGATTCAAGGA GCAATGC-3' <u>(SEQ ID NO:356)</u>	5' - CTGGAATTTCGC CTTGAAACTAC AAGTTTC-3' <u>(SEQ ID NO:357)</u>	
K559	KIAA0559	AB011131	AA766-870; PDZ1 (of 1)	Bam HI / Eco RI	N4-30	N267-240
	HYIFPHARIKITRDSKDHTVSGN GLGIRIVGGKEIPGHSGEIGAYI AKILPGGSAEQTGKLMEGMQVLE WNGIPLTSKTYEEVQSIISQQSG EAEICVRDLNLMSNS <u>(SEQ ID NO:310)</u>			5' - AAAGGATCCA CTACATCTT CCTCACG-3' <u>(SEQ ID NO:358)</u>	5' - TCACAATTGGAA TAGCATATGTA GGTCCAG-3' <u>(SEQ ID NO:359)</u>	
RGS12	human regulator of G- protein signalling 12	AF035152	AA35-103; PDZ domain 1 (of 1)	Bam HI / Eco RI	N2290-2312	N2623-2595
	PPPRVRSVEVARGRAGYGFTLSG QAPCVLSCVMRGSPADFVGLRAG DQILAVNEINVKKASHEDVVKLI GNSS <u>(SEQ ID NO:311)</u>			5' - TGGGATCCCG CCCCAAGGG TGGGGAG-3' <u>(SEQ ID NO:360)</u>	5' - AGGAATTCCCA ATTAATTTCAC TAC-3' <u>(SEQ ID NO:361)</u>	

K316	KIAA0316	AB002314	AA197-284; PDZ domain 1 (of 1)	Bam HI / Eco RI	158KIF	159KIR
			PPAPRKVEMRRDPVLGFFVAGS EKPVVVRSVTPGPSEGKLIIPGD QIVMINDEPVSAAPRERVIDLVR SCKESILLTVIQYPSPKRNSS <u>(SEQ ID NO:312)</u>	5' - AAAGGATCCC TCCGGCTCCT CGGAAG-3' <u>(SEQ ID</u> <u>NO:362)</u>	5' - TTAGAATTCTG ATTTGGGAGAA GGGTAAG-3' <u>(SEQ ID</u> <u>NO:363)</u> N866-839	

DVL1	human dishevelled segment polarity protein homolog	AF006011	AA248-340; PDZ domain 1 (of 1)	Bam HI / Eco RI	1 <sup>st</sup> PCR: 5SDVIFR
			QSTVLNIVTVTLNMERHHFLGIS IVGQSNDRGDGGIYIGSIMKGGA VAADGRRIEPGDMILLQVNNDVNFFEN MSNDDAVRVLREIVSQTGPISLT VAKCWEFIVTD <u>(SEQ_ID</u> <u>NO:313)</u>	5' - TCATCCAGAC TCATCCGGAA G-3' <u>(SEQ_ID</u> <u>NO:364)</u> N652-673	5' - GCTCATGTGTCAC TCTTCACCG- 3' <u>(SEQ_ID</u> <u>NO:365)</u> N1195-1174
				2 <sup>nd</sup> PCR, nested: 37DVF	2 <sup>nd</sup> PCR, nested: 38DVR
				5' - TCGGAATTCCC	5' - TCGGATCCA ACGGTCACTC TCAAAC-3' <u>(SEQ_ID</u> <u>NO:366)</u>
					N1029-N1004
					N723-747

TAX40	human tax interaction protein 40	AF028827	AA35-137; PDZ domain 1 (of 1)	Bam HI / Eco RI 5' -	136TF	137TR
			LLPETHRRVRLHKHGSDRPLGFY IRDGMSVRVAPQGLERVPGIFIS RLVRGGLAESTGLLAVIDEILEV NGIEVAGKTLDQVTDMMVANSHN LIVTVKPANQANSS ( <u>SEQ_ID</u> <u>NO:314</u> )	ACGGGATCCT ACTGCCTGAG ACCCACC-3' <u>(SEQ_ID</u> <u>NO:368)</u>	5' - ACGGAATTCCG CTGGTTGGCGG GCTTGAC-3' <u>(SEQ_ID</u> <u>NO:369)</u>	5' - ACGGAATTCCG CTGGTTGGCGG GCTTGAC-3' <u>(SEQ_ID</u> <u>NO:369)</u>
TIAM1	T- lymphoma invasion and metastasis inducing protein 1	NM_003253	AA1001-1088; PDZ 1 (of 1)	Bam HI / Eco RI 5' -	39TF	40TR
			HSIHIKEKSDTAADTYGEFSSLSSVE EDGIRLYVNNSVKETGLASKKGKGL KAGDEILEINNRAAADALNSSMLK DFLSQPSLGLIJLVRRTYPELEEEFIV TD ( <u>SEQ_ID</u> <u>NO:315</u> )	TCGGGATCCAC AGCATCCACA TTGAG-3' <u>(SEQ_ID</u> <u>NO:370)</u>	5' - TCGGAATTCCCT CCAGCTCGGGG T-3' <u>(SEQ_ID</u> <u>NO:371)</u>	5' - TCGGAATTCCCT CCAGCTCGGGG T-3' <u>(SEQ_ID</u> <u>NO:371)</u>
					N2995-3019	N3275-3253

MINT1	human X11 protein	L04953	AA717-894; PDZ domains 1-2 (of 2)	Eco RI / Eco RI	34MIF	20MR
			SENCKDVFIEKQKGEILGVVIVE SGWGSSILPTVITIANMMHGGPAEK SGKLNNIGDQIMSINGTSILVGLPL STCQSSIIGKLENQSRSRVKLNIIVRC PPVTTVLLIRRDPDLRYQLGFSVQN GIICSLMRGGIAERGGVRVGHRI IEINGQSVVATPHEKIVHILSNA <u>(SEQ_ID NO:316)</u>	5' - CGGAATTCTGG AAAACGTAA AGATG-3' <u>(SEQ_ID NO:372)</u>	5' - TCGGAATTCTGG CAGCCTGTACAA TCG-3' <u>(SEQ_ID NO:373)</u>	
K303	KIAA0303	Ab0002301	AA652-742; PDZ domain 1 (of 1)	Bam HI / Eco RI	152KIF	153KIR
			PHQPIVIHSSGKNYGFTIRAIRV YVGDSDIYTVDHVHNWNVVEEGSPA CQAGIKAQDLDLTHINGEPVHGLV HTEVIELLLIKSGNKVSITTTPFEE FIVTD <u>(SEQ_ID NO:317)</u>	5' - CTGGGATCCC ACATCAGCCG ATTGTGA-3' <u>(SEQ_ID NO:374)</u>	5' - TGTGAATTCTCAA ATGGGGTAGTA GTGATTG-3' <u>(SEQ_ID NO:375)</u>	N2237-2209
					N1948-1976	

CBP	Cytohesin binding protein HE	AF68836	AA85-176; PDZ domain 1 (of 1)	Bam HI / Eco RI 5' - CCTGGATCCA AAGAAAGCTT GTTACTGTG- 3' <u>(SEQ ID NO:318)</u> <u>(SEQ ID NO:376)</u>	235CYF 5' - TCAGAATTCCA TTAAGAGTCTC TATC-3' <u>(SEQ ID NO:377)</u> <u>(SEQ ID NO:376)</u> N535-510	236CYR 5' - CTCGAATTCCG TGCTCAGGCC GCCCTA-3', <u>(SEQ ID NO:379)</u> <u>(SEQ ID NO:378)</u> N246-274
MINT3	human MINT3	AF029110	AA11-52; PDZ domain 1 (of 1)	Bam HI / Eco RI 5' - ACTGGATCCC CGTCACCACC GCCATCATC- 3' <u>(SEQ ID NO:319)</u> <u>(SEQ ID NO:378)</u> N23-51	188MF 5' - CTCGAATTCCG TGCTCAGGCC GCCCTA-3', <u>(SEQ ID NO:379)</u> <u>(SEQ ID NO:378)</u> N165-138	189MR 5' - CTCGAATTCCG TGCTCAGGCC GCCCTA-3', <u>(SEQ ID NO:379)</u> <u>(SEQ ID NO:378)</u> N165-138
TAX2	human tax interaction protein 2	AF028824	AA54-140; PDZ domain 1 (of 1)	Bam HI / Eco RI 5' - AGGGATCCG CAAGGAGGTG GAGGTGTC- 3' <u>(SEQ ID NO:320)</u> <u>(SEQ ID NO:380)</u>	197 TF 5' - AGGGATCCG CAAGGAGGTG GAGGTGTC- 3' <u>(SEQ ID NO:380)</u> <u>(SEQ ID NO:381)</u>	198 TR 5' - TGTGGAATTCC TTGGGAGGCC CGTGAGC-3' <u>(SEQ ID NO:381)</u> <u>(SEQ ID NO:380)</u> N429-401

K561	KIAA0561	AB011133	AA948-1038; PDZ domain 1 (of 1)	Bam HI / Eco RI	N154-182	162KIR
			PPSLSTALARSTASACGRSASTW VIATSTLCTTSSGVWRTEAPP RR RACGLGTSSPSTGSQCGWCTW TSWSSCZRAATTRYPCGPQPWRIH RD <u>SEQ_ID NO:321</u>	5' - CCTGGATCCC CCCATCGTTA TCCACAGC- 3' <u>SEQ_ID</u> <u>NO:382</u>	5' - GAGGAATTCTC CAGGGCTGTGG TCCG- 3' <u>SEQ_ID</u> <u>NO:383</u>	

and Eco RI, Bam HI and Mfe I, or Eco RI only, Sma I only, or BamHI only (see TABLE 3). When more than one PDZ domain was cloned, the DNA portion cloned represents the PDZ domains and the cDNA portion located between individual domains. Precise locations of cloned fragments used in the assays are indicated in TABLE 3. DNA linker sequences between the GST portion and the PDZ domain containing DNA portion vary slightly, dependent on which of the above described cloning sites and approaches were used. As a consequence, the amino acid sequence of the GST-PDZ fusion protein varies in the linker region between GST and PDZ domain. Protein linkers sequences corresponding to different cloning sites/approaches are shown below. Linker sequences (vector DNA encoded) are bold, PDZ domain containing gene derived sequences are in italics.

- 1) **GST—BamHI/BamHI—PDZ domain insert**  
**Gly—*Ile*—PDZ domain insert**
- 2) **GST—BamHI/BglII—PDZ domain insert**  
**Gly—*Ile*—PDZ domain insert**
- 3) **GST—EcoRI/EcoI—PDZ domain insert**  
**Gly—*Ile*—Pro—Gly—Asn—PDZ domain insert (SEQ ID NO:258)**
- 4) **GST—SmaI/SmaI—PDZ domain insert**  
**Gly—*Ile*—Pro—PDZ domain insert**

Paragraph (TABLE 4) beginning at line 1 of page 60 has been amended as follows (see attached sheets).

Paragraph beginning at line 4 of page 66 has been amended as follows:

Other investigators have reported certain PL motifs important in PDZ binding, e.g., the C-terminal motifs S/T-X-V/I/L (for DLG1) and Y/F-Y/F-I/L/F for MPP1 (see, Doyle et al., 1996, Cell 85, 1067; Songyang et al., 1997, Science 275, 73). However, the reported motifs are not sufficiently specific (i.e. a large number of proteins meet these criteria yet are not necessarily actual PDZ ligands) and cover only a small number of PDZ proteins (approximately 10). The PRISM MATRIX can be used to determine ligand specificity and to deduce ligand binding motifs for any PDZ protein because it can precisely determine

CODE	PROTEIN NAME	GENBANK ACCESS	SEQUENCE	<u>SEQ ID NO:</u>
AA1L	Clasp-1		ISKATPALPTVSISSSAEV	<u>177</u>
AA2L	Clasp-2		ISGTPSTMVHGMTSSSSVV	<u>178</u>
AA3L	Clasp-4		CAISGTSSDRGYGSPRYAEV	<u>179</u>
AA4L	CD3n	M33158	SVFSIPTLWSPWPSSSSQL	<u>180</u>
AA5L-M*	CD4	M12807	SEKKTSQSPHRFQKTCSPI	<u>181</u>
AA6L	CD6	X60992	SPQPDSTDNDDYDDISAA	<u>182</u>
AA7L	CD34	M81104	QATSRNGHSARQHVVADTEL	<u>183</u>
AA9L	CD44	M69215	QFMTADETRNLQNVDMKIGV	<u>184</u>
AA10L	CD46 (Form 1)	M58050	KKGTYLTDETHREVKFTSL	<u>185</u>
AA11L	CD49E ( 4)	X06256	PYGTAMEKAQLKPPATSADA	<u>186</u>
AA12L	CD49F	X53586	HKAEIHAQPSDKERLTSADA	<u>187</u>
AA13L	CD95	M67454	KDITSDSENSNFRNEIQSLV	<u>188</u>
AA14L	CD97	X84700	TSGTGNQTRALRASESGI	<u>189</u>
AA15L	CD98	J02939	ERLKLEPHEGLLRFPYAA	<u>190</u>
AA16L	CD105	X72012	STNHSIGSTQSTPCSTSSMA	<u>191</u>
AA17L	VCAM1	M73255	ARKANMKGSYSLVEAQKSKV	<u>192</u>
AA18L	CD138	J05392	PKQANGGAYQKPTKQEEFYA	<u>193</u>
AA19L	CD148	D37781	ENLAPVTTFGKTNGYIA	<u>194</u>
AA20L	CD166	L38608	DLGNMEENKKLEENNHKTEA	<u>195</u>
AA22L	DNAM-1	U56102	TREDIYVNYPTFSRRPKTRV	<u>196</u>
AA23L-M*	FasL	U11821	SSKSksseesqtfglykl	<u>197</u>
AA25L	FceRIb	D10583	YSATYSELEDPGEMSPPIDL	<u>198</u>
AA28L	CDW125 (IL5R)	X62156	EVICYIEKPGVETLEDSVF	<u>199</u>
AA29.1L	CDW128A (IL8RA)	M68932	ARHRVTSYTSSSVNVSSNL	<u>200</u>
AA29.2L	CDW128B (IL8RB)	M73969	KDSRPSFVGSSSGHTSTTL	<u>201</u>
AA30L	LPAP	X81422	AWDDSSARAAGGQGLHVTAL	<u>202</u>
AA33L	KV1.3	AAC31761	TTNNNPNSAVNIKKIFTDV	<u>203</u>
AA34.2L	NMDA	NP000824	LNSCSNRRVYKKMPSIESDV	<u>204</u>
AA37L	Glycophorin C	AAA52574	QGDPAQDAGDSSRKEYFI	<u>205</u>
AA38L	Neurexin	AB011150	SSAKSSNKNKKNDKEYYY	<u>206</u>
AA39L	Syndecan-2	A33880	GERKPSSAAQKAPTKEFYA	<u>207</u>
AA40L	DOCK2	BAA13200	LASKSAAEGKQIPDSLSTDL	<u>208</u>
AA41L	CC CKR-1R	L09230	LERVSSTSPSTGEHELSAGF	<u>209</u>
AA42L	CC CKR-2	U03882	GKGKSIGRAPEASLQDKEGA	<u>210</u>
AA43L	CC CKR-3	HSU28694	LERTSSVSPSTAEPELSIVF	<u>211</u>
AA44L	CC CKR-4	X85740	DTPSSSYTQSTMHDHLHDAL	<u>212</u>
AA45L	BLR-1	S56162	PSWRRSSLSESENATSLTTF	<u>213</u>
AA47L	CD83	Z11697	VTSPNKHLGLVTPHKTELV	<u>214</u>
AA48L	CD62E	M30640	SSSQSLESQKPSYIL	<u>215</u>
AA49L	CD5	X04391	SMQPDNSSDSDYDLHGAQRL	<u>216</u>
AA55L	CD148	D37781	TIYENLAPVTTFGKTIA	<u>217</u>

\*The Sequence studied is mutated at positions >10 amino acids from C-terminus to increase water solubility and/or eliminate intramolecular disulfides.

sequences of amino acids that do or do not result in specific PDZ binding. In addition, the assay has revealed a significant of new PDZ domain binding motifs (i.e. PL motifs): C-terminal sequence of CD6, ISAA (SEQ ID NO:14); C- terminal sequence of CD49E, TSDA (SEQ ID NO:24); C- terminal sequence of CD49F, TSDA (SEQ ID NO:24); C-terminal sequence of CLASP-1-Clasp-1, SAEV (SEQ ID NO:289); C- terminal sequence of CLASP-4, YAEV (SEQ ID NO:228); C- terminal sequence of CD44, KIGV (SEQ ID NO:104); C-terminal sequence of IL5R, DSVF (SEQ ID NO:94); and C-terminal sequence of BLR-1, LTTF (SEQ ID NO:253). Identification of these novel PL sequences allows the definition of novel PL motifs (See **TABLE 5A**, *infra*). The specificity with which these novel motifs are defined is enhanced by the fact that the MATRIX reports both positive results (i.e. PDZ-PL) combinations that result in specific binding interactions) and negative results (i.e. PDZ-PL combinations that do not result in specific binding). For example, the C-terminal sequence of CD6, SAA and the C-terminal sequence of CD49E, SDA bind to the PDZ-domain polypeptide 41.8 while the related C-terminal sequence of CD166, TEA and C- terminal sequence of CD148, YIA do not. This identifies the novel PL motif (Motif 1, *infra*) of polypeptides terminating in alanine with serine at the -2 position and excludes polypeptides with threonine and tyrosine at the -2 position. This motif is therefore more specific than most previously identified motifs. Other novel motifs are described in **TABLE 5A**.

Paragraph beginning at line 9 of page 106 has been amended as follows:

**FIGURES 3A-H** show the use of peptides to inhibit PL-PDZ interactions using the G assay described *supra*. In **FIGURE 3A and B**, the inhibititon assays were carried out using GST fusion proteins containing PDZ domains from DLG1 or PSD95 (see *supra* and **TABLE 3**). Binding of biotinylated PL peptides for CLASP-2-Clasp 2, CD46, Fas, or KV1.3 (as listed in **TABLE 4**) was determined in the presence of various competitor peptides (at a concentration of 100 uM) or in the absence of a competitor (equalized as 100% binding). The competitor peptides were 8-mers peptides -having the sequence of C-terminus of CLASP-2 Clasp-2 (MTSSSSVV; SEQ ID NO:227), CD46 (REVKFTSL; SEQ ID NO:113), or Fas (TFFGLYKL; SEQ ID NO:83) (RNEIQSLV), a unlabeled 19-mer having the sequence of c-terminus of KV1.3 (i.e., non-biotinylated AA33L as listed in **TABLE 4** **TABLE 3**), or a peptide having the sequence of residues 64-76 of hemoglobin (Vidal *et al.*,

1999, *J. Immunol.* 163, 4811), i.e., an unrelated competitor. The binding of biotinylated peptide (10 uM for Fas and KV1.3, 20 uM for CLASP-2 Clasp-2 and CD46) to GST alone was subtracted from the binding to the fusion proteins to obtain the net signal for each experimental condition. This net signal was then normalized by dividing by the signal in the absence of competitor peptide and the data were plotted. Error bars indicated the standard deviation of duplicate measurements. Specific inhibition of CLASP-2 Clasp-2 PL-DLG PDZ binding was observed with the CLASP-2 8-mer, the CD46 8-mer, the Fas 8-mer-FAS 8-mer, and the KV1.3 KV13 peptide, but not in the absence of peptide or using an unrelated peptide.

Paragraph beginning at line 24 of page 106 has been amended as follows:

**FIGURES 3C-F** show similar assays using shorter peptides to inhibit (e.g., a 3-mer and a 5-mer). **FIGURES 3C-E** ~~Figures 3C-E~~ show binding of biotinylated PL peptides for CLASP-2 Clasp-2, CD46, Fas, or KV1.3, at the indicated concentration (as listed in **TABLE 3**) to GST fusion proteins containing PDZ domains from NeDLG, DLG1, or PSD95 in the absence or presence of 1 mM 3-mer peptide having the sequence of the C-terminus of Clasp 2 (SVV) (**TABLE 3**). -(Table 3). **FIGURE 3F** shows the effect on binding of a 5-mer CD49E peptide (ATSDA; SEQ ID NO:25) (ATSDA) to GST fusion proteins containing a PDZ domain from 41.8Kd.

Paragraph beginning at line 3 of page 109 has been amended as follows:

The C-terminal core sequence of CD49f is TSDA (SEQ ID NO:24) (SEQ ID NO:29). When naturally-occurring residues are added to the core sequence, LTSDA (SEQ ID NO:30), RLTSDA (SEQ ID NO:31), ERLTSDA (SEQ ID NO:32), and KERLTSDA (SEQ ID NO:33) may also be used to target a PDZ domain-containing protein in T cells.

Paragraph beginning at line 11 of page 109 has been amended as follows:

The C-terminal core sequence of CD83 is TELV (SEQ ID NO:248) (SEQ ID NO:248). When naturally-occurring residues are added to the core sequence, KTELV (SEQ

ID NO:249) (SEQ. ID. NO: 249), HKTELV (SEQ ID NO:250) (SEQ. ID. NO: 250), PHKTELV (SEQ ID NO:251) (SEQ. ID. NO: 251), and TPHKTELV (SEQ ID NO:252) (SEQ. ID. NO: 252) may also be used to target a PDZ domain-containing protein in T cells.

Paragraph beginning at line 21 of page 110 has been amended as follows:

The C-terminal core sequence of CLASP-1 is SAQV (SEQ ID NO:218) (SEQ. ID. NO: 218). When naturally-occurring residues are added to the core sequence, SSAQV (SEQ ID NO:219) (SEQ. ID. NO: 219), SSSAQV (SEQ ID NO:220) (SEQ. ID. NO: 220), ISSSAQV (SEQ ID NO:221) (SEQ. ID. NO: 221), and SISSSAQV (SEQ ID NO:222) (SEQ. ID. NO: 222) may also be used to target a PDZ domain-containing protein in T cells.

Paragraph beginning at line 25 of page 110 has been amended as follows:

The C-terminal core sequence of CLASP-2 is SSVV (SEQ ID NO:223) (SEQ. ID. NO: 223). When naturally-occurring residues are added to the core sequence, SSSVV (SEQ ID NO:224) (SEQ. ID. NO: 224), SSSSVV (SEQ ID NO:225) (SEQ. ID. NO: 225), TSSSSVV (SEQ ID NO:226) (SEQ. ID. NO: 226), and MTSSSSVV (SEQ ID NO:227) (SEQ. ID. NO: 227) may also be used to target a PDZ domain-containing protein in T cells.

Paragraph beginning at line 29 of page 110 has been amended as follows:

The C-terminal core sequence of CLASP-4 is YAEV (SEQ ID NO:228) (SEQ. ID. NO: 228). When naturally-occurring residues are added to the core sequence, RYAEV (SEQ ID NO:229) (SEQ. ID. NO: 229), PRYAEV (SEQ ID NO:230) (SEQ. ID. NO: 230), SPRYAEV (SEQ ID NO:231) (SEQ. ID. NO: 231), and GSPRYAEV (SEQ ID NO:232) (SEQ. ID. NO: 232) may also be used to target a PDZ domain-containing protein in T cells.

Paragraph beginning at line 33 of page 110 has been amended as follows:

The C-terminal core sequence of KV1.3 is FTDV (SEQ ID NO:238) (SEQ. ID. NO: 238). When naturally-occurring residues are added to the core sequence, IFTDV (SEQ ID NO:239) (SEQ. ID. NO: 239), KIFTDV (SEQ ID NO:240) (SEQ. ID. NO: 240), KKIFTDV (SEQ ID NO:241) (SEQ. ID. NO: 241), and IKKIFTDV (SEQ ID NO:242) (SEQ. ID. NO: 242) may also be used to target a PDZ domain-containing protein in T cells.

Paragraph beginning at line 3 of page 111 has been amended as follows:

The C-terminal core sequence of DOCK2 is STDL (SEQ ID NO:243) (SEQ. ID. NO: 243). When naturally-occurring residues are added to the core sequence, LSTDL (SEQ ID NO:244) (SEQ. ID. NO: 244), SLSTDL (SEQ ID NO:245) (SEQ. ID. NO: 245), DSLSTDL (SEQ ID NO:246) (SEQ. ID. NO: 246), and PDSLSTDL (SEQ ID NO:247) (SEQ. ID. NO: 247) may also be used to target a PDZ domain-containing protein in T cells.

Paragraph beginning at line 22 of page 111 has been amended as follows:

The C-terminal core sequence of Syndecan-2 is EFYA (SEQ ID NO:89) (SEQ. ID. NO: 258). When naturally-occurring residues are added to the core sequence, KEFYA (SEQ ID NO:259) (SEQ. ID. NO: 259), TKEFYA (SEQ ID NO:260) (SEQ. ID. NO: 260), PTKEFYA (SEQ ID NO:261) (SEQ. ID. NO: 261), and APTKEFYA (SEQ ID NO:262) (SEQ. ID. NO: 262) may also be used to target a PDZ domain-containing protein in B cells.

Paragraph beginning at line 26 of page 111 has been amended as follows:

The C-terminal core sequence of BLR-1 is LTTF (SEQ ID NO:253) (SEQ. ID. NO: 253). When naturally-occurring residues are added to the core sequence, SLTTF (SEQ ID NO:254) (SEQ. ID. NO: 254), TSLTTF (SEQ ID NO:255) (SEQ. ID. NO: 255), ATSLTTF (SEQ ID NO:256) (SEQ. ID. NO: 256), and NATSLTTF (SEQ ID NO:257) (SEQ. ID. NO: 257) may also be used to target a PDZ domain-containing protein in B cells.

Paragraph beginning at line 5 of page 114 has been amended as follows:

The C-terminal core sequence of CD105 is SSMA (SEQ ID NO:159). When naturally-occurring residues are added to the core sequence, TSSMA (SEQ ID NO:160), STSSMA (SEQ ID NO:161), CSTSSMA (SEQ ID NO:291) (~~SEQ ID NO:162~~) and PCSTSSMA (SEQ ID NO:162) (~~SEQ ID NO: 162~~) may also be used to target a PDZ domain-containing protein in endothelial cells.

Paragraph beginning at line 17 of page 114 has been amended as follows:

The C-terminal core sequence of VCAM1 is KSKV (SEQ ID NO:163) (~~SEQ ID NO: 233~~). When naturally-occurring residues are added to the core sequence, QKSKV (SEQ ID NO:164) (~~SEQ ID NO: 234~~), AQKSKV (SEQ ID NO:165) (~~SEQ ID NO: 235~~), EAQKSKV (SEQ ID NO:166) (~~SEQ ID NO: 236~~), and VEAQKSKV (SEQ ID NO:167) (~~SEQ ID NO: 237~~) may also be used to target a PDZ domain-containing protein in endothelial cells.

Paragraph beginning at line 23 of page 114 has been amended as follows:

Fc $\epsilon$ RI $\beta$ , CDw125, CDw128 and IL-8RB are transmembrane receptors expressed by mast cells, basophils and eosinophils. These receptors play a role in the activation of these cells to result in degranulation and histamine release in allergic reactions. The C-terminal core sequence of Fc $\epsilon$ RI $\beta$  is PIDL (SEQ ID NO:129) (~~SEQ ID NO:4~~). When naturally-occurring residues are added to the core sequence, PPIDL (SEQ ID NO:130) (~~SEQ ID NO:5~~), SPPIDL (SEQ ID NO:131) (~~SEQ ID NO:6~~), MSPPIDL (SEQ ID NO:132) (~~SEQ ID NO:7~~) and EMSPPIDL (SEQ ID NO:133) (~~SEQ ID NO:8~~) may also be used to target a PDZ domain-containing protein in mast cells. In addition, the residue E may be substituted with G to increase its binding affinity.

Paragraph beginning at line 31 of page 114 has been amended as follows:

The C-terminal core sequence of CDw125 is DSVF (SEQ ID NO:94) (SEQ ID NO:9). When naturally-occurring residues are added to the core sequence, EDSVF (SEQ ID NO:95) (SEQ ID NO:10), LEDSVF (SEQ ID NO:96) (SEQ ID NO:11), TLEDSVF (SEQ ID NO:97) (SEQ ID NO:12), and ETLEDSVF (SEQ ID NO:98) (SEQ ID NO:13) may also be used to target a PDZ domain-containing protein in mast cells.

Paragraph beginning at line 1 of page 115 has been amended as follows:

The C-terminal core sequence of CDw128 is SSNL (SEQ ID NO:69) (SEQ ID NO:14). When naturally-occurring residues are added to the core sequence, VSSNL (SEQ ID NO:70) (SEQ ID NO:15), NVSSNL (SEQ ID NO:71) (SEQ ID NO:16), VNVSSNL (SEQ ID NO:72) (SEQ ID NO:17), and SVNVSSNL (SEQ ID NO:73) (SEQ ID NO:18) may also be used to target a PDZ domain-containing protein in mast cells.

Paragraph beginning at line 5 of page 115 has been amended as follows:

The C-terminal core sequence of IL-8RB is STTL (SEQ ID NO:233) (SEQ ID NO:19). When naturally-occurring residues are added to the core sequence TSTTL (SEQ ID NO:234) (SEQ ID NO:20), HTSTTL (SEQ ID NO:235) (SEQ ID NO:21), GHTSTTL (SEQ ID NO:236) (SEQ ID NO:22) and SGHTSTTL (SEQ ID NO:237) (SEQ ID NO:23) may also be used to target a PDZ domain-containing protein in mast cells.

Paragraph beginning at line 10 of page 115 has been amended as follows:

The C-terminal core sequence of NMDA is ESDV (SEQ ID NO:263) (SEQ ID NO:263). When naturally-occurring residues are added to the core sequence, IESDV (SEQ ID NO:264) (SEQ ID NO:264), SIESDV (SEQ ID NO:265) (SEQ ID NO:265), PSIESDV (SEQ ID NO:266) (SEQ ID NO:266), and MPSIESDV (SEQ ID NO:267) (SEQ ID NO:267) may also be used to target a PDZ domain-containing protein in neuronal cells.

Paragraph beginning at line 14 of page 115 has been amended as follows:

The C-terminal core sequence of neurexin is EYYV (SEQ ID NO:268) (SEQ. ID. NO: 268). When naturally-occurring residues are added to the core sequence, KEYYV (SEQ ID NO:269) (SEQ. ID. NO: 269), DKEYYV (SEQ ID NO:270) (SEQ. ID. NO: 270), KDKKEYYV (SEQ ID NO:271) (SEQ. ID. NO: 271), and NDKKEYYV (SEQ ID NO:272) (SEQ. ID. NO: 272) may also be used to target a PDZ domain-containing protein in neuronal cells.

Paragraph beginning at line 19 of page 115 has been amended as follows:

The C-terminal core sequence of Glycophorin C is EYFI (SEQ ID NO:273) (SEQ. ID. NO: 273). When naturally-occurring residues are added to the core sequence, KEYFI (SEQ ID NO:274) (SEQ. ID. NO: 274), RKEYFI (SEQ ID NO:275) (SEQ. ID. NO: 275), SRKEYFI (SEQ ID NO:276) (SEQ. ID. NO: 276), and SSRKEYFI (SEQ ID NO:277) (SEQ. ID. NO: 277) may also be used to target a PDZ domain-containing protein.

Paragraph beginning at line 23 of page 115 has been amended as follows:

The C-terminal core sequence of CD148 is KTIA (SEQ ID NO:278) (SEQ. ID. NO: 278). When naturally-occurring residues are added to the core sequence, GKTIA (SEQ ID NO:279) (SEQ. ID. NO: 279), FGKTIA (SEQ ID NO:280) (SEQ. ID. NO: 280), TFGKTIA (SEQ ID NO:281) (SEQ. ID. NO: 281), and TTFGKTIA (SEQ ID NO:282) (SEQ. ID. NO: 282) may also be used to target a PDZ domain-containing protein in epithelial or myeloid cells.

Paragraph beginning at line 9 of page 138 has been amended as follows:

All peptides were chemically synthesized by standard procedures. The Tat-CD3 carboxyl terminus fusion peptide, (GYGRKKRRQRRRGPPSSSSGL, SEQ ID

NO:174); Tat-CLASP1 carboxyl terminus fusion peptide, (GYGRKKRRQRRRGSISSSAEV, SEQ ID NO:175); Tat-CLASP2 carboxyl terminus fusion peptide, (GYGRKKRRQRRRGMTSSSVV, SEQ ID NO:176); and Tat peptide, (GYGRKKRRQRRRG, SEQ ID NO:289 ~~SEQ ID NO:\_\_\_\_~~); were dissolved at 1 mM in PBS, pH 7, or dH<sub>2</sub>O. Stock MBPAc1-16 peptide, (AcASQKRPSQRHGSKYLA; SEQ ID NO:290), was dissolved at 5 mM. All peptides were aliquoted and stored at -80°C until tested.

Paragraph beginning at line 24 of page 140 has been amended as follows:

To detect such inhibition, it was necessary to synthesize an analogue of the CLASP2peptide AA2L that (1) retained similar DLG1 binding properties and (2) would not itself generate a signal in the assay selected to measure inhibition. Because most molecular interactions between PDZ proteins and their ligands involve only the C-terminal 6 amino acids of the ligand, an eight amino acid variant of the CLASP-2 peptide, MTSSSSVV (SEQ ID NO:227), was anticipated to retain similar DLG1 binding properties as the 20 amino acid AA2L CLASP-2 peptide. This eight amino acid CLASP-2 peptide (lacking a functional label) was therefore synthesized and purified by standard techniques as described *supra*. When 100 uM of the (functionally unlabeled) eight amino acid CLASP-2 peptide and 20 uM of the biotin-labeled AA2L CLASP-2 peptide were added simultaneously to DLG1 in a variant of the "G" assay (described *supra*), the binding of the labeled AA2L CLASP-2 peptide was, as predicted, inhibited by greater than 50% (**FIGURE 3A**). An analogous experiment in which the labeled AA2L CLASP-2 peptide was replaced with another labeled DLG1 ligand, labeled AAI3L Fas peptide demonstrated similar inhibition by the eight amino acid CLASP-2 peptide (**FIGURE 3A**). Thus, an effective inhibitor of DLG1-ligand binding (i.e. the eight amino acid CLASP-2 peptide MTSSSSVV; SEQ ID NO:227) with a known potency range (order of magnitude 21 uM) was designed based on knowledge of the affinity, 21 uM, with which a particular labeled ligand, the CLASP-2 peptide AA2L; bound to DLG1.